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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/643,319

08/19/2003

Michael D. Ruff

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EXAMINER

OH, SIMON J

ART UNIT

PAPER NUMBER

1618

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

01/03/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/643,319

Applicant(s)

RUFF ET AL.

Examiner

Simon J. Oh

Art Unit

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 43-53 and 55-57 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43-53 and 55-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Papers Received

Receipt is acknowledged of the applicant's amendment, response, and petition for extension of time, all received on 12 October 2006.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 56 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 56 recites the limitation "of Claim 1" in the first line of the claim. There is insufficient antecedent basis for this limitation in the claim, as Claim 1 is cancelled. However, in order to advance prosecution of this claim, it will be assumed that the applicant intended to refer to Claim 43, the first listed independent claim pending in this case.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of Claims 43-53 and 55 under 35 U.S.C. 103(a) over Norling *et al.* is maintained.

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Claims 56 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Norling *et al.* (U.S. Patent No. 5,958,458) in view of Ekwuribe *et al.* (U.S. Patent Application Publication No. 2003/0050228)

The Norling *et al.* patent teaches a pharmaceutical multiple unit formulation in the form of coated cores. The core material is selected from various materials that include calcium carbonate, calcium silicate, calcium magnesium silicate, calcium phosphate, and kaolin (See Abstract). Various substances may be applied as coatings to the cores, including waxes, hydrogenated oils, and glyceryl monostearate. The coating material may be admixed with excipients that include colloidal silicon dioxide, talc, and magnesium stearate. The coating material may further comprise plasticizers, such as castor oil, mineral oil, and coconut oil (See Column 9, Line 41 to Column 10, Line 57). Film coatings comprising polymers such as ethylcellulose may be included in the disclosed composition (See Column 9, Lines 43-50). The disclosed composition may be embodied in various formulations, including powders, granules, tablets, as well as liquid formulations (See Column 13, Lines 29-36). The cores may also comprise an active substance, which may be coated onto the surface of the cores (See Column 11, Lines 57-67). The active substance may be selected from various broad categories of agents, including insulin (See Column 7, Lines 60-67). The formulations disclosed in the patent are described as being very suitable for oral administration in various solid forms (See Column 12, Lines 39-42). The patent discloses examples where inert cores are prepared and where varying amounts of various coating materials are applied to these cores (See Example 1A to Example 10). In view of the prior art disclosure of the core material being coated with various excipients

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such as hydrogenated oils and magnesium stearate, it is the position of the examiner that this disclosure reads on what the applicant was chosen to define as a permeation enhancer.

The Norling *et al.* patent does teach insulin among a list of suitable pharmaceutical substances, but it does not specifically teach insulin in the form of hexyl insulin monoconjugate-2 polydisperse, also known as HIM2.

The Ekwuribe *et al.* reference discloses methods for the treatment of diabetes where oral compositions of insulin drugs are administered, for the purpose of administering insulin to a subject in need thereof through routes that are more convenient than the traditional method of subcutaneous administration of insulin (See Claim 1; and Sections 0003 to 0017). To this end, the Ekwuribe *et al.* reference discloses insulin polypeptides that are suitable for oral administration, such as HIM2 (See Sections 0133 to 0134). Solid pharmaceutical formulations for oral administration such as powders and granules are disclosed (See Section 0145).

It is the position of the examiner that the instantly claimed invention is made obvious by the collective disclosure of the prior art. As the Norling *et al.* patent teaches pharmaceutical compositions suitable for oral administration having an inert core that may be coated with an active agent such as insulin, one of ordinary skill in the art would be motivated to substitute insulin taught in the Norling *et al.* patent with the insulin polypeptides disclosed in the Ekwuribe *et al.* reference, since such insulin drugs are disclosed as being better suited for the oral administration of insulin. As both prior art references are drawn to oral pharmaceutical formulations that contain an insulin drug, they are considered analogous to one another and one of ordinary skill in the art would thus have a reasonable expectation of success in combining the

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references to arrive at the instantly claimed invention. The instantly claimed invention is therefore prima facie obvious.

Response to Arguments

Applicant's arguments filed 12 October 2006 have been fully considered but they are not persuasive.

The applicant's sole argument is centered on the applicant's interpretation of the prior art concerning the structure of the particulate pharmaceutical formulation disclosed therein. The applicant's evaluation of the prior art makes it clear that the applicant is of the opinion that the prior art teaches only a particulate pharmaceutical formulation that contains a core that is a blended mixture of an active agent and an inert material, where the prior art is drawn to a particulate pharmaceutical formulation having a core that is coated with an active agent.

The applicant's analysis is based on an incorrect interpretation of the prior art, having seen fit to narrowly characterize the entire prior art disclosure based on only one embodiment of the several that are disclosed therein. As the examiner set forth previously in the prior art rejection of record, the Norling *et al.* patent teaches that in a particular embodiment, the cores may be fashioned such that an active agent is coated onto the surface of the cores, which fit into and do not conflict with the description of the disclosed invention cited by the applicant on Page 6 of the response received on 12 October 2006. Specifically, on Column 11, Lines 65-67 of the Norling *et al.* patent, it specifically states that "the active substance is present in a layer on the outer surface of the uncoated or coated cores", which reads on the limitations of the instantly

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claimed invention. The applicant's analysis of the prior art is therefore erroneous, and the prior art rejection of record is maintained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Simon J. Oh whose telephone number is (571) 272-0599. The examiner can normally be reached on M-F 8:30 am to 5:00 pm.

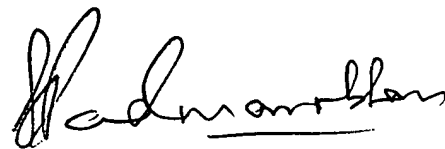
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Simon J. Oh
Examiner
Art Unit 1618

sj0

A handwritten signature in black ink, appearing to read 'Sreeni Padmanabhan', with a horizontal line underneath the name.

**SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER**